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Exposure misclassification due to residential mobility during pregnancy



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ABSTRACT

Objectives: Pregnant women are a highly mobile group, yet studies suggest exposure error due to migration in pregnancy is minimal. We aimed to investigate the impact of maternal residential mobility on exposure to environmental variables (urban fabric, roads and air pollution (PM₁₀ and NO₂)) and socio-economic factors (deprivation) that varied spatially and temporally.

Methods: We used data on residential histories for deliveries at ≥ 24 weeks gestation recorded by the Northern Congenital Abnormality Survey, 2000–2008 ($n = 5399$) to compare: (a) exposure at conception assigned to maternal postcode at delivery versus maternal postcode at conception, and (b) exposure at conception assigned to maternal postcode at delivery versus mean exposure based on residences throughout pregnancy.

Results: In this population, 24.4% of women moved during pregnancy. Depending on the exposure variable assessed, 1–12% of women overall were assigned an exposure at delivery >1 SD different to that at conception, and 2–25% assigned an exposure at delivery >1 SD different to the mean exposure throughout pregnancy.

Conclusions: To meaningfully explore the subtle associations between environmental exposures and health, consideration must be given to error introduced by residential mobility.

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Introduction

Epidemiological studies carried out at the ecological level, or using routinely collected health data, often assign exposure to an individual's residence at a single time point, such as birth, hospitalisation or death. This approach fails to account for individuals who might have migrated into or out of the population or for periodic spells away from a residence where levels of exposure are likely to be different from those experienced at home. Such migrations could result in exposure error or misclassification, reduced study

power, and may result in biased risk estimates (Armstrong, 1998; Blair et al., 2007; Khoury et al., 1988).

Many environmental epidemiological studies of birth outcomes assign a measure of exposure based on maternal residential location at delivery because this information is readily available. The relatively short period between exposure and disease manifestation should mean that studies on congenital anomalies are less prone to migration bias, as there is less time in which the population can migrate. However, there is now a significant body of literature showing that pregnant women are a highly mobile group, with 10–30% of women moving residence during pregnancy (Bell and Belanger, 2012; Canfield et al., 2006; Fell et al., 2004; Hodgson et al., 2009; Khoury et al., 1988; Shaw and Malcoe, 1992; Zender et al., 2001).

Theoretical papers on the implications of residential mobility during pregnancy on the ability to detect environmental teratogens (Khoury et al., 1988) and impacts of differential mobility (Schulman et al., 1993) remain relevant, and a study showing the impact of mobility on real-life exposure scenarios and on

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environmental risk factors likely to confer small, but important increases in risk, is overdue. In this paper we investigate the impact of residential mobility during pregnancy on the measurement of exposure to a range of environmental factors previously explored in aetiological research (for example area-level measures of deprivation (Dibben et al., 2006; Janevic et al., 2010), land cover (e.g. urban/rural classifications) (Hillemeier et al., 2007; Langlois et al., 2010), road density/proximity to roads (Yorifuji et al., 2011) and air pollutants (Dugandzic et al., 2006; Hansen et al., 2009; Xu et al., 2011)), and quantify the exposure error likely to be introduced into a study reliant on maternal residential location at delivery as a proxy for residential location at conception and throughout pregnancy.

Materials and methods

The Northern Congenital Abnormality Survey (NorCAS) is a prospective, population-based registry covering the former UK northern health region, which includes north east England and north Cumbria (Fig. 1). This region comprises a population of about three million, with approximately 32,000 births each year over the study period 2000–2008, of which approximately 826 births each year (2.6%) included a major congenital anomaly and were therefore recorded in NorCAS. Data are collected on congenital anomalies occurring in late miscarriages (>20 weeks gestation), in live births and stillbirths, and in terminations of pregnancy for foetal anomaly after prenatal diagnosis at any gestation. The NorCAS follows the European Surveillance of Congenital Anomalies guidelines for inclusion on the register and classification of anomalies (see <http://www.eurocat-network.eu/content/EUROCAT-Guide-1.3-Chapter-3.3-Jan2012.pdf>) and codes anomalies according to the WHO International Classification of Diseases version 10. Cases are reported to the register from multiple sources to ensure a high case ascertainment, as described previously (Boyd et al., 2005; Richmond and Atkins, 2005). For this study, data on all pregnancies with a congenital anomaly delivered between 01 January 2000 and 31 December 2008 were extracted from NorCAS, although this dataset was subsequently restricted to those with a gestation at delivery of ≥ 24 weeks (a viable delivery), to allow better comparison with pregnancies resulting in a healthy delivery. If more than one baby in a multiple pregnancy has a congenital anomaly, each case is included on NorCAS. However, for this study, the pregnancy was counted as the ‘case’ so each pregnancy was counted only once.

The NorCAS contains addresses for women at both booking appointment (average gestational age 13 weeks in the UK) and delivery. To obtain more detailed information on residential history, the NorCAS data were linked to the UK National Health Service National Strategic Tracing Service records. Linkage was achieved using several data fields, including the mother’s date of birth, National Health Service number, surname and residential postcode. Address at delivery was confirmed and updated as required. Date of conception was calculated from the date and gestation at booking (available within the NorCAS), and address details at this date, as well as any other residences during the index pregnancy (with dates of when the women moved to and from this address) available from the National Strategic Tracing Service were extracted to provide address at conception, and enable residential history throughout pregnancy to be established. All addresses were geocoded based on the address postcode centroid, the geographic centre of a collection of approximately 15 adjacent households making up the postcode. Within the study area the average distance between nearest neighbouring postcodes was 104 m, max 6.2 km, though this distance varied considerably between urban and rural areas (for example, in Newcastle Local Authority (a predominantly urban

Table 1

Social and environmental variables assigned to maternal residential postcodes to explore the impact of residential mobility during pregnancy on characterisation of exposure.

Socio-economic status

1. Index of Multiple Deprivation at Super Output Area level

Data source	Office for National Statistics
Variable type	Continuous and quintile, area level
Spatial resolution	Super Output Area
Temporal resolution	n/a (data for 2007 used for whole study period)
2. Index of Multiple Deprivation at Local Authority level

Data source	Office for National Statistics
Variable type	Continuous and quintile, area level
Spatial resolution	Local Authority
Temporal resolution	n/a (data for 2007 used for whole study period)

Land cover

3. % Continuous Urban Fabric within 500 m buffer of postcode

Data source	CORINE land cover 2000v8 ^a
Variable type	Continuous and dichotomous, individual level
Spatial resolution	100 m
Temporal resolution	n/a (data from 2000 used for whole study period)
4. % Discontinuous Urban Fabric within 500 m buffer of postcode

Data source	CORINE land cover 2000v8 ^a
Variable type	Continuous and quintile, individual level
Spatial resolution	100 m
Temporal resolution	n/a (data from 2000 used for whole study period)

Roads

5. Total length (m) of roads (motorways, A and B roads) within 500 m buffer of postcode

Data source	Strategi 2011 ^b
Variable type	Continuous and quintile, individual level
Spatial resolution	1 m
Temporal resolution	n/a (data from 2011 used for whole study period)

Air pollution

6. Annual background PM10

Data source	DEFRA Ambient Air Quality Assessment (UKAAQA) ^c
Variable type	Continuous and quintile, individual level
Spatial resolution	1 km grid square
Temporal resolution	Annual mean, 2001–2008
7. Daily NO₂

Data source	DEFRA Automatic Urban and Rural Network ^d
Variable type	Continuous and quintile, individual level
Spatial resolution	Nearest monitor (for those living within 15 km of a monitor)
Temporal resolution	Daily mean (averaged over first trimester), 2000–2008

^a <http://www.eea.europa.eu/data-and-maps/data/corine-land-cover-2000-clc2000-100-m-version-8-2005>.

^b www.ordnancesurvey.co.uk/oswebsite/docs/user-guides/strategi-user-guide.pdf.

^c <http://uk-air.defra.gov.uk/data/pcm-data>.

^d <http://uk-air.defra.gov.uk/networks/network-info?view=aurn>.

area) the average distance was 49 m, max 1.16 km, in contrast in Tynedale (rural authority) the average distance was 255 m, max 7.95 km). Grid references were obtained from the Office for National Statistics Postcode Directory (<http://edina.ac.uk/ukborders/>).

To establish the impact of residential mobility during pregnancy on exposure classification, we assigned to each woman’s postcode at delivery and conception a measure of exposure to a variety of environmental factors, and, based on residential history, a measure of mean exposure throughout pregnancy weighted according to proportion of the pregnancy spent at each postcode. These variables include typical environmental factors explored in aetiological epidemiological research. We deliberately chose factors that were (a) readily available, (b) varied in terms of their spatial and/or temporal resolution, and (c) able to be assigned at the individual and/or area level. These variables are described in Table 1.

For deprivation, we used the 2007 Index of Multiple Deprivation, which comprises 38 indicators of deprivation spread across seven domains (income deprivation; employment deprivation; health deprivation and disability; education, skills and training

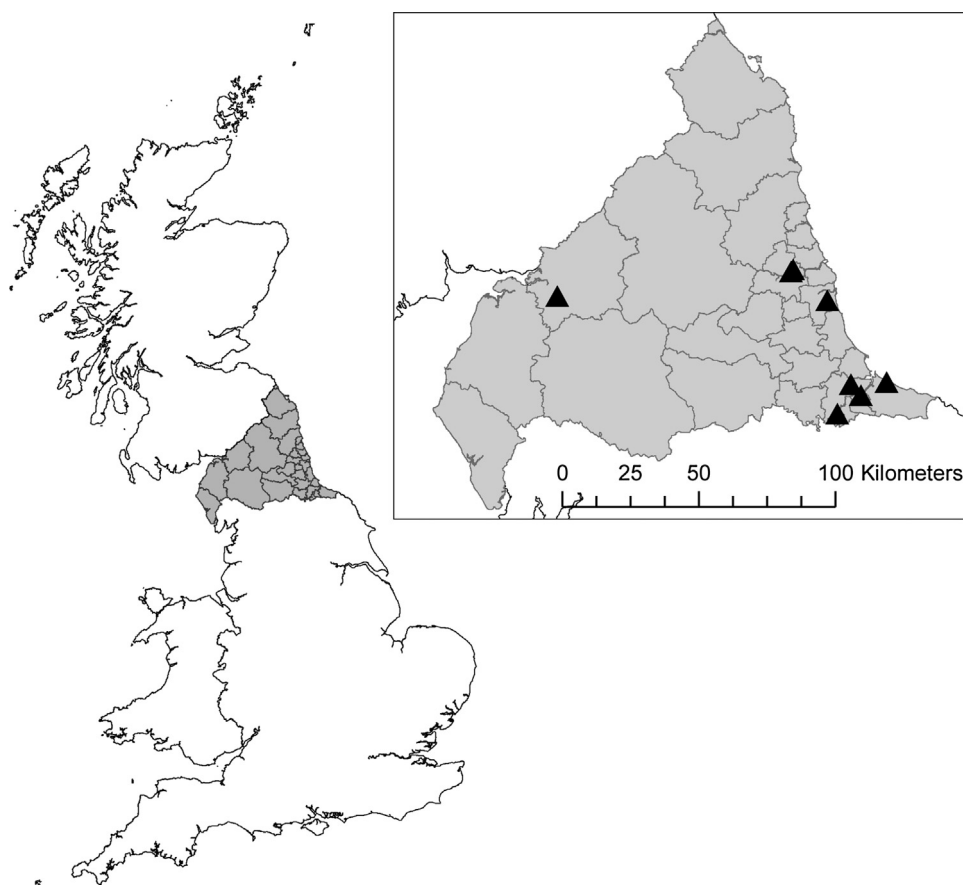


Fig. 1. Map showing the geographic coverage of the Northern Congenital Abnormality Survey (NorCAS) (shaded area), and inset showing the locations of the DEFRA Automatic Urban and Rural Network NO₂ monitors (black triangles).

deprivation; barriers to housing and services; living environment deprivation; and crime) (Noble et al., 2008). This index was extracted at the area level for (1) lower layer Super Output Areas, a census based unit with a mean population of 1500, and (2) at Local Authority level, an administrative unit with a mean population of 140,000. We assigned to each postcode the deprivation score of the Super Output Area or Local Authority that contained that postcode centroid.

The CORINE land cover classes are discriminated mainly by physiognomic attributes (shape, size, colour and pattern) of landscape objects (natural, modified, cultivated and artificial), as recorded on satellite images (de Lima, 2005). The smallest surfaces mapped correspond to 25 ha, and the scale of the output was fixed at 1:100,000, giving a location precision of 100 m. In the Continuous urban fabric land class, most of the land is covered by buildings, roads and artificially surfaced areas which cover almost all the ground. The Discontinuous urban fabric land class is also characterised by most of the land being covered by structures, but here the buildings, roads and artificially surfaced areas are associated with vegetated areas and bare soil (www.eea.europa.eu/publications/COR0-part1/download). Continuous urban fabric (3) and Discontinuous urban fabric (4) were assessed at the individual level; we assigned to each postcode the proportion of each land cover class within a 500 m buffer of the postcode centroid.

For roads (5), assessed at the individual level, we used OS Strategi data to assign to each postcode the total metres of motorways, A roads (large-scale transport links within or between areas) and B roads (which feed traffic between A roads and smaller roads on the network) within a 500 m buffer of the postcode centroid.

For annual background particulate matter (particles less than 10 µm in diameter (PM₁₀)) (6), we used DEFRA Ambient Air Quality data (background pollution maps at 1 km × 1 km resolution) to assign to each postcode at conception and delivery the annual mean PM₁₀ concentration for year of conception. To calculate the mean PM₁₀ exposure through pregnancy, each postcode was assigned the annual mean(s) for the year(s) of residence, which were then weighted according to proportion of the pregnancy spent at each postcode.

Nearest monitor daily mean nitrogen dioxide (NO₂) concentrations (7), a variable with limited spatial variability due to the small number of monitors across the study region (at conception, six sites in the north east provided data for 98.4% of the women, see Fig. 1), was assessed at the individual level (for those women living within 15 km of a monitor (an arbitrary cut-off)). We used DEFRA Automatic Urban and Rural Network data (the main network used for compliance reporting) to assign to each postcode at delivery and conception the mean NO₂ exposure for the first trimester (first 90 days of each pregnancy), as well as mean exposure throughout pregnancy based on residential history.

The level of agreement between (a) exposure at conception assigned to postcode at delivery versus postcode of conception, and (b) exposure at conception assigned to postcode at delivery versus mean exposure throughout pregnancy based on residential history, was assessed by a range of measures. These included: (i) as continuous variables using Pearson correlation co-efficient (*R*), (ii) as quintiles using Cohen's kappa co-efficient (*K*) to take into account agreement occurring by chance, with quintiles based on equal percentiles at conception/mean exposure throughout pregnancy, apart from continuous urban fabric which, due to granularity

Table 2

Agreement between exposures (a) at conception, assigned to postcode at delivery versus postcode at conception, and (b) at conception assigned to postcode at delivery versus mean through pregnancy based on residential history, for all women, non-movers and those who moved during pregnancy.

Variable	All women				Non-movers				Movers			
	<i>n</i>	<i>R</i>	<i>K</i>	Accuracy	<i>n</i>	<i>R</i>	<i>K</i>	Accuracy	<i>n</i>	<i>R</i>	<i>K</i>	Accuracy
1. Super Output Area Deprivation Score												
a) Delivery versus conception	5391	0.89	0.83	0.91	4078	1	1	1	1313	0.57	0.30	0.62
b) Delivery versus mean through pregnancy	5396	0.96	0.90	0.95	4078	1	1	1	1318	0.86	0.59	0.81
2. Local Authority Deprivation Score												
a) Delivery versus conception	5391	0.92	0.94	0.97	4076	1	1	1	1313	0.69	0.75	0.89
b) Delivery versus mean through pregnancy	5393	0.98	0.96	0.98	4076	1	1	1	1317	0.90	0.84	0.94
3. % Continuous Urban Fabric												
a) Delivery versus conception	5399	0.81	0.83	0.96	4080	1	1	1	1319	0.33	0.32	0.84
b) Delivery versus mean through pregnancy	5399	0.94	0.91	0.97	4080	1	1	1	1319	0.75	0.68	0.89
4. % Discontinuous Urban Fabric												
a) Delivery versus conception	5399	0.84	0.79	0.90	4080	1	1	1	1319	0.34	0.19	0.59
b) Delivery versus mean through pregnancy	5399	0.95	0.88	0.94	4080	1	1	1	1319	0.79	0.49	0.77
5. Metres roads within 500 m												
a) Delivery versus conception	5399	0.83	0.80	0.88	4080	1	1	1	1319	0.36	0.20	0.52
b) Delivery versus mean through pregnancy	5399	0.94	0.86	0.93	4080	1	1	1	1319	0.78	0.44	0.71
6. Annual PM10												
a) Delivery versus conception	4396	0.95	0.91	0.96	3290	1	1	1	1106	0.81	0.65	0.85
b) Delivery versus mean through pregnancy	4396	0.88	0.64	0.84	3290	0.90	0.66	0.86	1108	0.81	0.55	0.80
7. NO ₂												
a) Delivery versus conception	3373	0.95	0.98	0.98	2571	1	1	1	802	0.81	0.89	0.92
b) Delivery versus mean through pregnancy	3365	0.74	0.27	0.75	2571	0.76	0.26	0.75	794	0.67	0.28	0.73

R = Pearson correlation co-efficient, with exposures assessed as continuous variables.

K = Cohen's kappa co-efficient, with exposures as quintiles, apart from continuous urban fabric which was explored as a dichotomous variable.

Accuracy = exposure at delivery assumed correct if within one standard deviation of exposure assigned at conception/throughout pregnancy.

in the data, was explored as a dichotomous variable (i.e. exposed or not exposed to any continuous urban fabric within 500 m of postcode), or (iii) assessed for accuracy, where exposure at conception assigned to delivery postcode was assumed 'correct' if it was within one standard deviation (SD) of the exposure assigned at conception postcode/mean exposure throughout pregnancy.

To explore the likelihood of introducing differential exposure misclassification, independent sample *t*-tests were used to compare mean exposure at conception for non-movers versus movers. In addition, paired sample *t*-tests were used to compare mean exposure at conception assigned to postcode of delivery versus postcode of conception, and mean exposure at conception assigned to postcode of delivery versus mean exposure throughout pregnancy based on residential history. *p* Values <0.05 were taken as statistically significant.

Data were linked in GIS ESRI ArcMap 10.0 and analysed using IBM SPSS Statistics Version 20.

Ethical approval

The NorCAS, as part of the British Isles Network of Congenital Anomaly Registers, has National Information Governance Board (now Health Research Authority) exemption from a requirement for consent for inclusion on the register under section 251 of the National Health Service Act (2006) and has ethics approval (09/H0405/48) to undertake studies involving the use of its data.

Results

NorCAS registered 7432 deliveries during 2000–2008. Of these, 7231 (97.3%) were able to be linked to women represented in the National Strategic Tracing Service data, with the remaining 201 deliveries not able to be linked, likely due to missing or mismatched data, or due to their mother not being registered with a GP and therefore not appearing in the National Strategic Tracing Service dataset. Postcode at conception and delivery was able to be geocoded for 6972/7432 deliveries (93.8%). When further restricted to represent pregnancies with a gestational age at delivery of ≥ 24

weeks (a viable delivery), 5399 (72.7%) pregnancies remained. Of these, 1319 women (24.4%) moved during pregnancy. With respect to the timing of moves, the mean number of days after gestation before the first move was 112 days (16 weeks); a little over half of the women who moved (686/1319; 52%) did so during their first trimester, 378 (28.7%) moved during their second trimester, and 255 (19.3%) moved during their third trimester. The mean and median moving distance amongst movers were short, at 19.26 and 1.85 km respectively, with 72.5% of women moving within 5 km.

When looking at all women, the majority of whom did not move, there was, as expected, good agreement between (a) exposure at conception assigned to postcode at delivery versus postcode at conception, and (b) exposure at conception assigned to postcode at delivery versus mean exposure throughout pregnancy based on residential history (Table 2). The level of agreement was similar when variables were assessed using Pearson correlation co-efficient (*R*), Cohen's kappa co-efficient (*K*) or assessed for accuracy (i.e. within one standard deviation (SD)). For the air quality variables PM10 (6) and NO₂ (7), which exhibit temporal variability, the agreement between exposure at delivery and mean throughout pregnancy was weaker, likely due to the underlying temporal trends in pollution levels, which showed a decline over the time period studied. For women who moved during pregnancy, the agreement between exposures at conception assigned to postcode at delivery versus conception, or postcode at delivery versus mean exposure throughout pregnancy was much weaker.

The relatively good agreement, overall, between exposures at conception assigned to delivery versus conception postcode, and at delivery postcode versus residences throughout pregnancy, hides the fact that, at the individual level, substantial differences in exposure do occur.

For some variables, a substantial proportion of women would be assigned a different exposure at conception if postcode at delivery was used in lieu of postcode at conception, or in lieu of residential history throughout pregnancy. Fig. 2 shows the difference in exposure at conception assigned to maternal postcode at delivery versus conception, and, for PM10, the difference in exposure at conception assigned to maternal postcode at delivery versus exposure

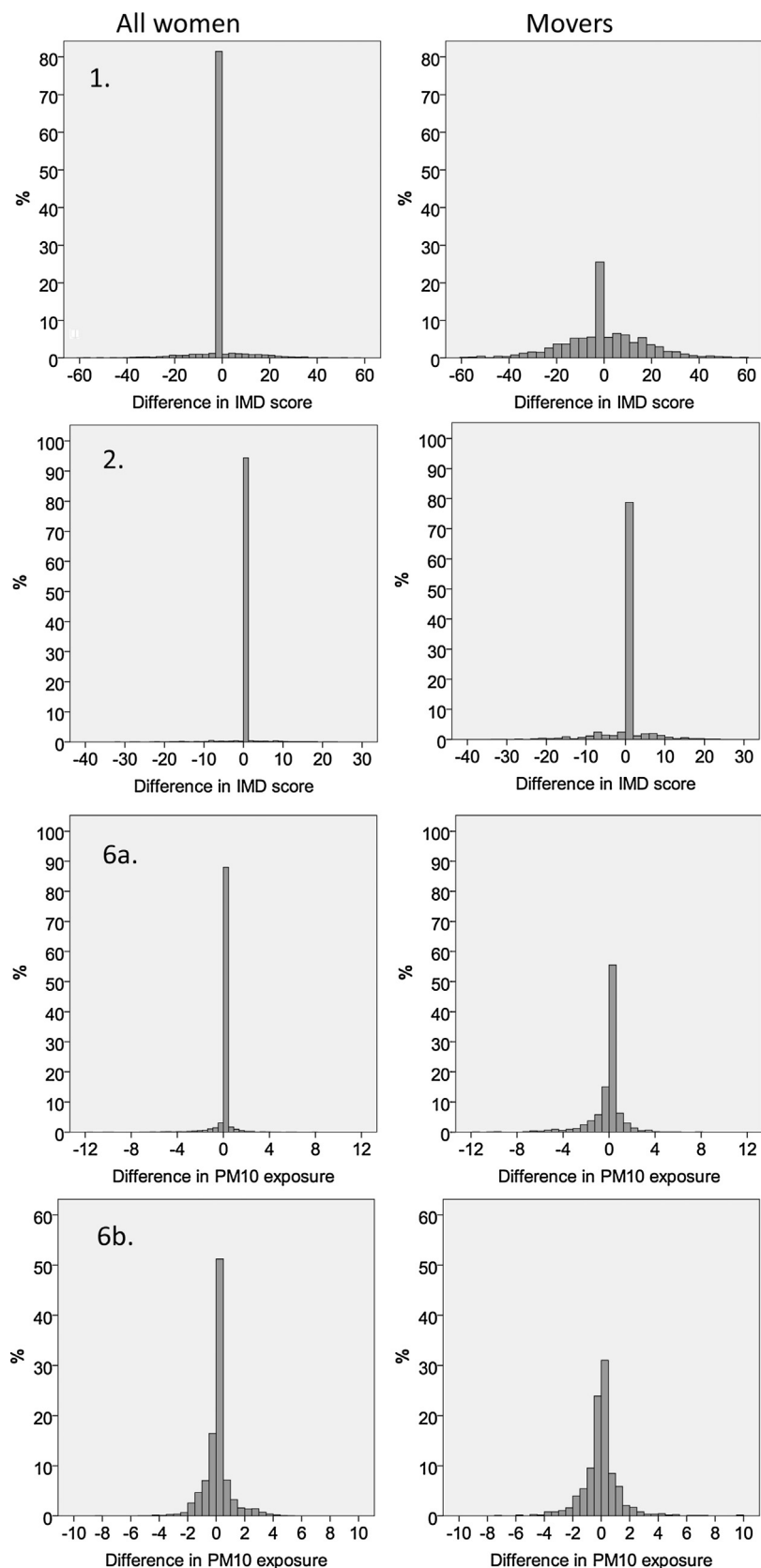


Fig. 2. Histograms showing the difference in exposure at conception assigned to maternal postcode at delivery versus conception for all women (left hand side) and movers (right hand side) for: (1) Deprivation at Super Output Area level, (2) Deprivation at Local Authority level, (6a) PM10; and (6b) the difference in PM10 exposure at conception assigned to maternal postcode at delivery versus exposure throughout pregnancy based on residential history.

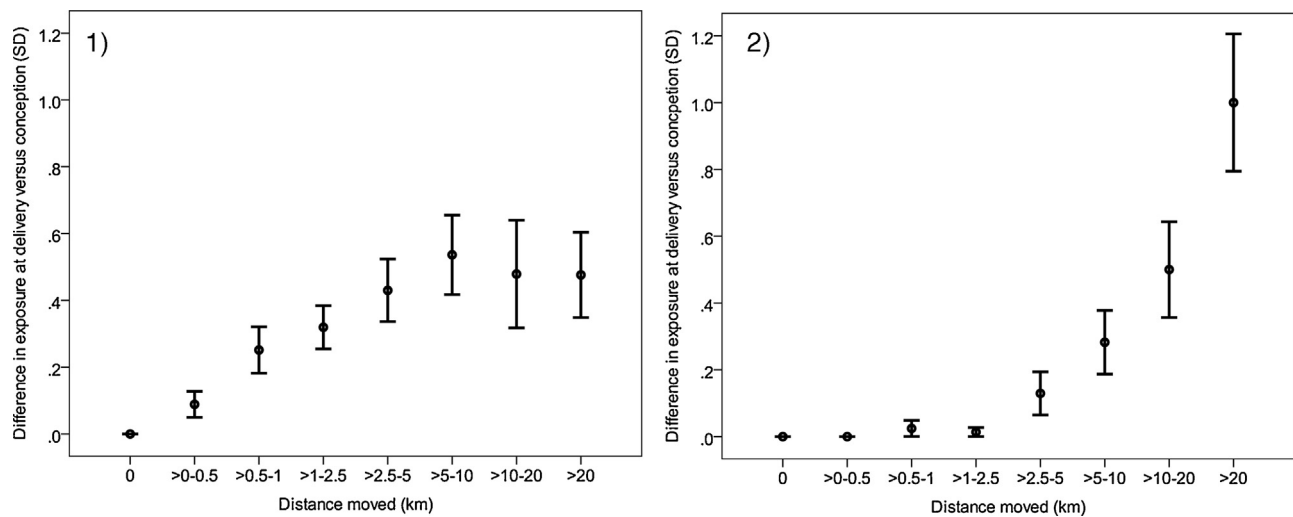


Fig. 3. Change in Deprivation Score (in SD) between maternal postcode at conception and delivery by distance moved for (1) Deprivation Score assigned to Super Output Area, and (2) Deprivation Score assigned to Local Authority.

throughout pregnancy based on residential history, for all women and for those moving during pregnancy. For spatially varying exposures assigned at the area level (e.g. Deprivation at the Super Output Area (1) and Local Authority level (2)) or individual level (e.g. annual mean PM₁₀ (6a)) we see that, overall, relatively few women are assigned a different exposure. In these instances, it is only those women moving during pregnancy who would be assigned a different exposure. It is evident that the scale at which the exposure is measured is important; far more women are assigned a different deprivation score when measured at the Super Output Area level (1) than at the Local Authority level (2). Where women move only short distances (>70% within 5 km), they are more likely to move to a different Super Output Area than to a different Local Authority (Fig. 3). Nonetheless, for those women who do move during pregnancy, their exposure at conception assigned to delivery postcode can be quite different from that assigned to conception postcode. For exposures with spatial and temporal variability (PM₁₀, NO₂), there were substantial differences in exposure at conception versus exposure throughout pregnancy, for all women and for those moving during pregnancy (e.g. Fig. 2 (6b)).

While our previous study showed that movers in this cohort tended to be younger and to live in more deprived areas (Hodgson et al., 2009), independent sample *t*-tests show that, at conception, movers tend to live in more deprived, urban areas, near to a greater density of roads, and with lower air quality (as measured by PM₁₀ and NO₂) (Table 3).

Furthermore, as shown in Table 4, movers tended, on average, to move to less deprived, less urban areas (although paired sample *t*-tests indicate that these differences were not statistically significant), with lower road density ($p=0.05$), and higher air quality (>0.01).

Discussion

We investigated the impact of residential mobility during pregnancy on how exposure to a range of real-life social and environmental factors, which exhibited spatial and temporal variability at a range of scales, is characterised. We aimed to assess the degree of exposure error/misclassification that might be introduced into a study using address at delivery as a proxy for maternal residence (and, therefore, foetal exposure) at a more aetiological relevant period, such as at conception, or throughout pregnancy. We have shown that mean exposures, even amongst movers, may not significantly differ when assigned to address at delivery versus

conception. However, comparing mean exposures hides the fact that increases in exposure in some are offset by decreases in others; depending on the scale at which exposure is measured and/or the scale at which it exhibits heterogeneity, substantial numbers of women may in fact have been assigned very different exposures at delivery versus conception address.

Previous studies addressing the issue of mobility have reported that exposure does not differ significantly if using maternal residential address at delivery rather than address at conception, implying that use of the former is adequate to estimate exposure during the critical early stages of pregnancy (Chen et al., 2010; Lupo et al., 2010). Chen et al. (2010) explored the impact of mobility on exposure to ozone and PM₁₀ in 1324 women in New York, 16.5% of whom moved during pregnancy. There was a good agreement between exposure quartiles measured at conception and delivery (Kappa ≥ 0.78 , $p < 0.01$), however the spatial resolution of the exposure data was low; the study area was divided into only seven air monitoring regions of between 247–11,790 and 628–10,760 square miles for ozone and PM₁₀ respectively. The scale at which the exposure data were available may have played a role in shaping the observed agreement between these exposure variables at conception and delivery; very few women ($n=33$) moved between monitoring regions (Chen et al., 2010). Lupo et al. (2010) explored the impact of mobility on the assignment of census tract-level estimates of ambient benzene at the delivery and conception addresses of 141 pregnancies affected by a neural tube defect and 591 unaffected control pregnancies. Although 30% of case and 24% of control mothers moved during pregnancy, there was good agreement between quartiles of benzene exposure at delivery and conception across the study population (Kappa = 0.78, $p < 0.01$), which the authors attributed to the fact that the residential movements were generally within a short distance. Nonetheless, 17% of women were misclassified (if we take exposure at conception to be the gold standard), and 4.5% were misclassified by two or more quartiles (Lupo et al., 2010).

The theoretical papers on this topic discuss the issue of whether residential mobility is likely to introduce non-differential or differential exposure error. Ritz et al. (2007) found the association between CO exposure and preterm birth strengthened (although confidence intervals widened) when their analyses were restricted to women who had not changed residence throughout pregnancy, suggesting that non-movers suffer less from exposure misclassification/error, and that in this instance, the misclassification/error was likely to be non-differential. Madsen et al. (2010) studied

Table 3

Exposure at conception for women who did not, versus those who did, move during pregnancy.

Exposure	Non-movers		Movers		<i>p</i> ^a
	<i>n</i>	Mean	<i>n</i>	Mean	
1. Super Output Area Deprivation Score	4078	31.75	1314	35.13	<0.01
2. Local Authority Deprivation Score	4076	28.15	1314	28.17	0.91
3. % Continuous Urban Fabric within 500 m	4080	4.61	1319	5.61	<0.05
4. % Discontinuous Urban Fabric within 500 m	4080	62.51	1319	63.21	0.45
5. Metres roads within 500 m	4080	734.25	1319	782.21	0.03
6. Annual PM10 (µg/m ³)	3290	14.34	1106	14.64	<0.01
7. First trimester NO ₂ (µg/m ³)	2571	28.36	838	29.22	<0.01

^a Independent sample *t*-tests.

exposure misclassification in a cohort of 25,229 pregnant women, 28% of whom moved during pregnancy. Women who moved during pregnancy had a lower traffic pollution exposure after moving compared to women who did not move. In addition, women who moved were younger, more often nulliparous and of non-western ethnicity, had lower education, and their offspring had on average 47.5 g lower mean birth weight compared to those women who did not move during pregnancy (Madsen et al., 2010) suggesting the possibility of differential exposure error. In the NorCAS cohort, women who moved during pregnancy also tended to be younger and live in more socio-economically deprived areas (Hodgson et al., 2009) in keeping with findings from other populations (Bell and Belanger, 2012), and, as shown here, movers also tend to live near a higher density of roads and in areas with higher levels of air pollution. These women tend to have lower exposure at delivery than at conception. If women are moving from areas with higher exposure at conception to areas with lower exposure at delivery, then it seems likely that using postcode at delivery will result in exposure in this group being underestimated, and, if the characteristics of those who move are associated with the health outcome of interest, then we risk introducing differential bias into our study, potentially biasing our risk estimates towards or away from the null.

The extent of exposure error introduced by assigning exposure to the address at delivery will depend on the degree of spatial and temporal variability the exposure exhibits, the scale at which this heterogeneity acts, and the resolution at which the exposure is studied. Residential mobility is less likely to introduce exposure error into a study assessing exposures which display heterogeneity over a large geographic scale (e.g. Deprivation measured at the Local Authority area (2) versus Super Output Area level (1)). Until recently it could have been argued that the spatial/temporal resolution of our exposure data was the limiting factor in environmental epidemiological studies and that the bias introduced by residential mobility only a minor concern. We are currently experiencing a step change in our ability to measure and/or model environmental exposures over large areas and at a high resolution (Beelen et al., 2009; Vienneau et al., 2010), but the benefits of such improvements

will only be fully realised once we are better able to capture details of how people interact with this exposure surface. Capturing and incorporating better data on aetiologically relevant exposure periods, and on where people reside at these times is a first, but important step, in linking people to the changing exposure environment they inhabit.

There are several limitations to consider when interpreting our findings. Firstly, the cohort studied was derived from a congenital anomaly dataset, so these findings may not be generalisable to all pregnancies, the majority of which result in a healthy infant. That said, there is no particular reason to believe these women will behave very differently with respect to residential mobility compared to women experiencing healthy pregnancy outcomes in the wider population from which our sample was drawn, as supported by evidence from case-control studies where mobility was similar for cases and controls (Bell and Belanger, 2012), and from a re-analysis of these data restricted to term deliveries (≥ 37 weeks) which produced essentially the same output (data not shown). Secondly, we have focussed on exposure error/misclassification due to residential mobility. It should be noted that this is only one aspect of a much wider issue relating to measuring and assigning meaningful exposures. Research questions obviously vary study by study, but we are usually trying to assess the impact of the biologically relevant dose at the target organ of interest (Blair et al., 2007). Given the difficulty of achieving this ideal, certainly in large populations and for exposures for which we have no or inadequate biological markers, we compromise and instead try to associate environmental concentrations near (or often rather far) from where someone lives (at birth, diagnosis, hospitalisation, death) to the health outcome of interest. This approach fails to account for inward or outward migration, or for daily or periodic spells away from a residence where levels of exposure are likely to differ from those experienced at home. Clearly there are many layers of exposure error introduced into this scenario before we start to concern ourselves about where someone actually lived at the aetiologically critical time.

Detailed data on residential histories are not routinely collected in the UK, despite their value for linking environmental exposures

Table 4

Exposure at conception assigned to postcode at delivery versus postcode at conception, and exposure at conception assigned to postcode at delivery versus mean exposure throughout pregnancy based on residential history, for women who moved during pregnancy.

Exposure	<i>n</i>	Mean exposure		<i>p</i> ^a	Pregnancy	<i>p</i> ^b
		Conception	Delivery			
1. Super Output Area Deprivation Score	1313	35.11	34.92	0.70	34.99	0.87
2. Local Authority Deprivation Score	1313	28.17	28.39	0.11	28.21	0.01
3. % Continuous Urban Fabric	1319	5.61	5.15	0.37	5.52	0.21
4. % Discontinuous Urban Fabric	1319	63.21	63.08	0.89	63.12	0.94
5. Metres roads within 500 m	1319	782.21	738.30	0.05	754.39	0.20
6. Annual PM10 (µg/m ³)	1106	14.64	14.42	<0.01	14.46	0.36
7. NO ₂ (µg/m ³)	802	29.12	28.61	<0.01	28.46	0.43

^a Paired sample *t*-test of difference between exposure at conception assigned to postcode at delivery versus conception.^b Paired sample *t*-test of difference between exposure at conception assigned to postcode at delivery versus mean exposure throughout pregnancy.

and health. These findings highlight the importance of collecting such data, and we encourage health registers to introduce relevant data fields to enable these data to be collected in the future. Where collecting data on full residential histories is not possible, data on length of time in residence, or whether a move took place during the time window of interest (e.g., during pregnancy) would enable an assessment of the potential impact of mobility on measures of risk. Where data on mobility are not available, researchers are urged to consider the likely impacts of residential mobility on their exposure estimates, for instance by considering the spatial and temporal heterogeneity of the exposure, and the scale at which it is measured. An understanding of the study population is also crucial, as for certain health end points e.g. those associated with maternal age, socio-economic deprivation etc., there is a possibility that mobility will introduce differential misclassification. Given the complex issues outlined above, pregnancy offers a relatively straight forward opportunity to study the impact of mobility on exposure error; for risk factors that may confer a health risk years or even decades after exposure, it is even more important that these sources of exposure error are studied and their impacts understood.

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